ON THE EXTRUSION

OF THE

MORPHOLOGICAL ELEMENTS OF THE BLOOD.

THE PHYSICAL PRINCIPLES CONCERNED,

AND THE RELATION WHICH SUCH EXTRUDED ELEMENTS BEAR TO PUS AND TO THE SO-CALLED FIBRINOUS EXUDATION OF INFLAMMATION.

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ON THE EXTRUSION OF THE MORPHOLOGICAL ELEMENTS OF THE BLOOD.

THE PHYSICAL PRINCIPLES CONCERNED, AND THE RELATION WHICH SUCH EXTRUDED ELEMENTS BEAR TO PUS AND TO THE SO-CALLED FIBRINOUS EXUDATION OF INFLAMMATION.

HISTORY OF THE SUBJECT.

In the year 1858 the illustrious pathologist, Professor Virchow of Berlin, spoke as follows, "There can at the present time be no longer any doubt as to the vascular system being everywhere closed by membranes. In these it is not possible to descry any porosity. Even the minute pores which have recently been observed in different parts, have not, up to the present time, met with their counterparts in the capillary membrane; and when the porosity of this membrane is spoken of, the expression can only be admitted in a physical sense, as applying to invisible, really molecular interstices. A film of collodion is not more homogeneous, nor more continuous, than the membrane of a capillary. A series of possibilities which used to be admitted, as that, for example, the continuity of the capillary membrane did not exist at certain points, simply falls to the ground. A transudation or diapedesis of the blood through the walls of the vessels, without the occurrence of any rupture, cannot for an instant be admitted; and although we cannot in every individual case point out the exact site of the rupture, it is notwithstanding quite inconceivable that the blood, with its corpuscles, should be able to pass through the walls in any other way than through a hole in them. This is such a very natural deduction from ascertained histological facts, that all discussion upon the point is impossible. Within the true capillary region, there is nothing further worthy of notice in the vessels than the nuclei I have previously mentioned, which correspond to the longitudinal axis of the vessel, and are so

imbedded in its membrane, that it is impossible to discover any traces of a surrounding cell wall. The capillary membrane is seen to be quite uniform, absolutely homogeneous and continuous."*

In 1867, nine years later, Professor Cohnheim, also of Berlin, published some remarkable researches, affirming that he had seen both the red and the white corpuscles making their way through the walls of the capillaries, apparently without rupture, into the surrounding tissues; and also that in inflammation, supervening upon irritation experiments, he had seen the white corpuscle become adherent to the wall of the vein, make its way through the wall, and appear on the outside as the pus corpuscle. Very considerable interest was created by the statements of Cohnheim, and his experiments were repeated and corroborated by eminent physiologists and pathologists in all parts of the world.

It is a curious circumstance in the history of the subject, that, twelve years prior to the asseveration of Virchow that such things were impossible, and twenty-one years anterior to the researches of Cohnheim, an English physiologist of great repute had forestalled the necessity both of the statement and counter-statement of these illustrious German observers. Without wishing to detract in the least from the importance of Dr. Cohnheim's re-discovery, it would ill become me, as the pupil of one, now no more, who once laboured in our midst, and who but eleven short years ago by his great and practical knowledge of physiological science, inspired me, however feebly, to follow in his footsteps in the culture and advancement of his much loved science, to be silent at the present juncture. In a word, I feel that I should be recreant in my duty and unworthy so great a master, did I not once for all unhesitatingly assert the claim of Dr. Augustus Waller to all the credit that may accrue from this discovery.

In the twenty-ninth volume of the "Philosophical Magazine," (1846), in the numbers for October and November, will be found two laborious papers which amply show how much this keen-sighted original worker was in these matters in advance of his time.

The first of these papers, entitled "A microscopic examination of some of the principal tissues of the animal frame, as observed in the tongue of the living frog, toad, &c.," left the hands of its author, September 21st, 1846, and the second paper, entitled "Microscopic observations on the perforation of the capillaries by

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* "Cell. Pathology," p. 113. (Chance.)

the corpuscles of the blood, and on the origin of mucus and pus-globules," is dated October 15th of the same year.

Not only had this investigator observed the escape of both the red and white corpuscles from the capillary vessels, but it is quite clear that he fully appreciated the important bearing of the observation upon pathology, for in his first paper we find him saying, "Recent observations have enabled me to decide the much agitated question as to the formation of pus, and its origin from the extravasation of the colourless or spherical corpuscles from the capillaries." Postponing the full elucidation of the subject to a future occasion, he nevertheless proceeds to give two observations.

The first experiment which Dr. Waller relates, is one in which he observed the white corpuscles escaping from the vessels in the mesentery of a toad, which had been dead for three hours, and the abdominal cavity and cellular tissues of which were found distended by a limpid dropsical collection of serum, containing numerous white corpuscles and a few blood discs; and he states that the only traces observable of their points of exit were curved indentations in the vessel of the same size as the corpuscles, and a solution in the continuity of the vessel at these points.

In the second experiment he used the living frog's tongue, and in this case both the red and white corpuscles, but the latter in by far the greatest number, escaped through the walls of the capillaries, whilst no appearance of rupture could be seen in any of the vessels. After the experiment had lasted about two hours, thousands of these corpuscles were seen scattered over the membrane, with scarcely any red discs. The process by which they passed out of the vessels could be best observed in a capillary containing stationary blood corpuscles. Generally at a slight distance from it some extravasated corpuscles could be detected, and at the nearest opposite point of the tube a small concave depression was presented. Frequently near this depression, numerous corpuscles were collected within the tube, as if about to follow those which had escaped. These were frequently agitated by a movement of oscillation which showed that there was no open point in the tube. In other spots some of these corpuscles were seen protruding half out of the vessel. When however the current re-occurred in a vessel presenting these appearances, the depression and unevenness quickly disappeared, and no trace of the corpuscular extravasation could be seen, except the presence of the corpuscles themselves. "I consider therefore," says Dr. Waller, "as established—(1) the passage of these corpuscles *de*

toute pièce through the capillaries, and (2) the restorative power in the blood, which immediately closed the aperture thus formed."*

In the second communication, page 397, entitled "Microscopic observations on the perforation of the capillaries by the corpuscles of the blood, and on the origin of mucus and pus globules," Dr. Waller shows most conclusively the identity of the white corpuscles of the blood with those of mucus and pus.

As to the manner in which the corpuscles escape from the vessels, Dr. Waller does not seem to have arrived at any more satisfactory conclusions than those who have succeeded him. He however points out that it is not connected with the life of the animal, as it is observed to take place after death. He suggests that "it may be due to a solvent action of the corpuscle upon the structures composing the wall of the vessel."

It is clear from all this that my illustrious predecessor and much revered master had observed and published as early as 1846, all those facts, which, re-discovered by Cohnheim, are about to exert an important influence upon the pathological thought of this age.

The experiments of Cohnheim have been performed principally upon the mesentery and foot of the frog. For web experiments a female is selected, as in the male the presence of pigment cells obscures the view. When the mesentery is used a large frog must be chosen.

Cohnheim's plan is to induce paralysis of the entire animal without rapidly destroying life, and to this end he injects under the skin from three to five minims of a solution of Woorara, containing one grain of the poison to a fluid ounce of water. This produces complete motor paralysis in about half an hour.

This preliminary condition being achieved, a glass plate sufficiently large to support the frog is taken, and to this is attached a very thin disc of cork with a hole in the centre. The abdomen of the

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* The following is Dr. Waller's description of the mode of escape. "In some instances the manner in which the corpuscle escaped from the interior of the tube could be distinctly followed; that part of the tube in contact with the external side of the corpuscle gradually disappeared, and at nearly the same time might be seen the formation of a distinct line of demarcation between the inner segment of the corpuscle and the fluid parts of the blood in contact with it. Any slight agitation was then capable of disengaging the corpuscle from the vessel to which it was now external, and in its place a concave depression remained, which appeared sufficiently protected by some membrane as to oppose effectually the exit of the discs and the fluid part of the blood." Page 399.

frog is now opened, the mesentery being carefully drawn out and stretched over the aperture in the disc of cork, and moistened from time to time by the application of a little artificial serum composed of albumen one part, common salt one tenth part, and water ten parts.

The following phenomena then take place: the arteries are first seen to contract, then gradually dilate, until in about an hour and a half they attain their maximum. The current at first becomes more rapid, then gradually retarded, and in about two hours from the commencement a movement of oscillation takes place preparatory to the occurrence of comple stasis. It is during this stage that the corpuscles, especially the white ones, may be seen to escape from the vessels, principally from the small veins, but also from the capillaries. In this experiment the stasis which occurs is believed to be the result of inflammation, produced by exposure of the serous membrane to the air, and the white corpuscles will be seen to pass out in far greater numbers than the red ones.

The second experiment of Cohnheim's is simply a variation of Weber's form of stasis as induced by strangulation of a limb, and which I showed in 1862* to be altogether a different kind of stasis

* Confusion has been introduced into the question of stasis as related to inflammation, by neglecting to discriminate between the various forms of stasis, of which there are four:—

(1) If the frog's web be exposed to certain irritants, (*e.g.* vapour of chloroform,) the arteries are so constricted that the heart force is temporarily shut off from the capillaries, which become packed by the reflux of blood from the veins. This form of stasis is dissipated immediately on the cessation of the arterial constriction. The blueness of the extremities consequent upon exposure to cold is probably dependent upon the same mechanism.

(2) The second form of stasis depends upon such enfeeblement of the heart's action as interferes with the due propulsion of blood into the extreme vessels. It also disappears upon the re-establishment of a sufficient propulsive power.

(3) The third form is that described by H. Weber, as follows: "If a limb (of a frog) be strangulated, there arises in its web, within four to eight hours, without any irritation being applied, a stasis which is identical with inflammatory stasis, except that after sixty hours' duration it will be dissipated as soon as the circulation is set free." The removal of this form of stasis by the re-establishment of the circulation distinguishes it from inflammatory stasis and shows its relation to the forms already described.

(4) The fourth form of stasis is producible (artificially) by the application of irritants, and has for its specific characteristics—

a) It is readily induced when the heart-force is unimpaired and the blood-channels are free;

from that homogeneous form which accompanies true inflammatory action. A portion of skin is removed from tho inner part of the groin, so as to exposo the femoral vein, around which a ligature may bo tied, or othor means adopted for arresting the circulation in tho vein ; practically it is found better to tako up a portion of the musclo with tho vein.

The immediate effect of the application of the ligature is to retard the stream of blood and to cause dilatation of the veins, the current gradually becoming slower and slower, until tho usual oscillating movements commence, preparatory to the occurrence of stasis. The blood corpuscles are seen to be collected in masses, while a few solitary individuals lie attached to the parietes of the vessels. The wall now becomes pouched and sometimes the corpuscles may be seen to pass out even during the occurrence of stasis in the vessel. When, however, the vein is released from the ligature the process takes place rapidly, and red corpuscles may be seen in every stage of transit through the walls: some, adherent by a slender process to the inner wall, vibrate backward and forward in consequence of repeated blows, received from successive corpuscles passing along in the stream ; others are firmly impacted in the walls ; and others again are only slightly adherent to the outer wall, or are found in the surrounding tissues. The web must be occasionally moistened and not allowed to become inflamed if it can possibly be avoided.*

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b) It requires hours or even days for its dissipation, or it may even be irresolvable;

c) It presents under the microscope a homogeneous appearance as if the vessels had been injected with tinted size or gelatine. The outlines of the corpuscles are undistinguishable. I call this "homogeneous" or "inflammatory" stasis.—Proceedings Royal Society, 1862.

* The fact that adhesiveness of the corpuscles was produced in the vessels of the web, is I think, a sufficient evidence that all the precautions taken failed to prevent the occurrence of the initial phenomena of inflammation. These earlier changes must be regarded as the primary effects of irritation, by which we mean that a part or structure is subjected to active influences other than those which normally operate upon it. The following observations of Professor Lister as bearing upon this point are worthy of the utmost consideration:—"Thus if a large vein happened to run through the spot upon which the mustard was placed, it became in time choked with a crimson mass of corpuscles in that part of its extent which lay beneath the mustard ; but immediately beyond in both directions, the blood in it contained no more than the usual proportion of corpuscles, or sometimes considerably less ; and these moved freely to and fro when the web was touched,

An able paper upon this subject was contributed last year to the British Association by Dr. Caton of Liverpool.* This author noticed—

(1) A slight dilatation of the vessels, making the exposed mesentery redder to the naked eye.

(2) A general retardation of the blood-flow, commencing in the veins and capillaries, and, when complete stasis had occurred in

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whereas those within the area remained fixed." Again, "Another important fact which was brought out by this class of experiments is, that mere quiescence of the blood in the vessels of a healthy part fails to induce aggregation of the red corpuscles. In the parts which had not been subjected to irritation, the corpuscles exhibited no trace of adhesiveness; and though completely at rest they were nowhere seen to be grouped together. . . . . On one occasion when examining the tissues of the web of a frog under chloroform, the limb being kept steady by a string tied tightly round the thigh, so as completely to arrest the circulation, I was particularly struck with the want of adhesiveness in the red corpuscles; so much so that as the foot had been kept moist without circulation for about three hours, I suspected that it must have imbibed water, which, when mixed with blood outside the body, destroys altogether the adhesiveness of the red corpuscles. This, however, proved to be a mistake, for having occasion to administer more chloroform, I applied it on a piece of lint of considerable size without taking the usual precaution of protecting the foot from the vapour, and left it so for about a quarter of an hour. On re-examination of the web, the red corpuscles were found to possess mutual adhesiveness, and in the larger vessels were grouped together into masses with considerable spaces of clear liquor sanguinis, just as in the best marked forms of aggregation in frog's blood outside the body."—Lister, on "The Early Stages of Inflammation." Pages 667-8.

As to the ease with which irritation is induced, Professor Lister remarks as follows:—"In perfect health the colourless corpuscles are as free from adhesiveness as the red discs, but like them assume that property in a degree proportionate to the amount of irritation to which the part has been subjected. When the irritation has been very slight, the white corpuscles, which are susceptible of much greater adhesiveness than the red, (as we learn from examining blood outside the body,) acquire some tendency to stick to the vascular parietes, while the red discs still move on in a manner generally regarded as consistent with health, though really lagging slightly behind the liquor sanguinis, and consequently presenting themselves in somewhat abnormal proportion."—Page 670, ibid.

As adhesion of the corpuscles must be regarded as one of the earlier phenomena which occur in the chain of circumstances constituting inflammation, we are bound to consider inflammatory conditions to have been present in Cohnheim's experiments upon webs.

* Contributions to the Cell-Migration Theory, by Richard Caton, M.D., "Edinburgh Journal of Anatomy and Physiology," No. VII., November 1870.

these, advance and regress of the corpuscles in the arteries, corresponding to every systole and diastole.*

(3) The white cells, when first observed after the operation, (opening of peritoneum,) were being carried along in the general stream in the veins generally occupying the "lymph space," where they could be traced rolling along at a somewhat slower pace than that of the red globules. After a time the white corpuscles became less circular in outline, and showed a tendency to adhere to the walls of the veins; later still, large numbers of the white cells were deposited from the stream, and covered the surface of the veins, and partially so of the capillaries. When the arterial current became slow, a few were also seen deposited in the arteries.

Some of the most interesting of Dr. Caton's observations were made upon the tadpole, and he found—

(1) That migration of the blood-cells takes place much easier, and to a far greater extent, in it than in the frog, and that in a congested state of the circulation corpuscles rapidly escape from the vessels at any part of their course.

(2) The vessels have indistinctly defined walls, and appear as though they were little more than channels hollowed out in the jelly-like substance of the tail.

(3) Any interference with the return of venous blood produces migration of red corpuscles very quickly, as Cohnheim has shown to occur in the foot of the frog when the femoral vein is tied. (Vide note, page 6.)

(4) If any injury, or the irritation produced by a constrained position, has produced that peculiar softened and plastic condition of the white cells in which they adhere to the walls of the veins, and

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* "Stasis generally occurs first at the venous radicles, because here the *vis a tergo* is weaker."

"If in a frog's web homogeneous stasis has occurred in the venous radicles so as completely to prevent the passage of blood into the veins, the current in the capillaries and supplying arteries might naturally be expected to be brought to a stand, as it certainly would be if the walls of the capillaries removed from the immediate seat of the obstruction were impervious; but so far from this being the case, the blood brought to the part is seen to pass on in a perfectly regular manner without the slightest rebound. This absence of rebound is an evidence that the liquor sanguinis is passing through the vascular parietes at the same rate it is being propelled into the obstructed vessels. It is not till the capillaries become packed with corpuscles, and the circulation is confined to the arterial trunk, that any rebound after ventricular contraction becomes apparent."—Proceedings Royal Society, August 28th, 1862.

if a coating of white cells has in consequence lined the veins before congestion occurs, the white cells migrate in the place of the red. White cells may be seen to escape from a vein, and red ones from an adjoining vessel, the latter often forming upon the vessel sides clump-like masses of adherent corpuscular matter.*

(5) The sizes of the apertures through which the corpuscles pass appear to be variable, sometimes appearing to be narrow, at other times the cell sinks through the wall without undergoing much change of form.

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* In these experiments the tadpole was laid upon its side in the stage trough with a cover-glass resting on its tail, and after being in this position for an hour, as a rule, both red and white corpuscles were seen to begin to migrate. It is admitted that general feverishness, as indicated by increased action of the heart, was induced, but it was stated that no appearance of local irritation existed. As further on in the paper it is admitted that, when either general fever or local inflammation exists, the white corpuscles are attracted to the sides of the vessel and rapidly deposited, forming often a complete coating to the veins, it is presumable that in the case where local irritation was supposed to be absent, this adhesiveness of the white corpuscles existed. Professor Lister states, and I think with great correctness, that the adhesiveness of the white corpuscle is invariably an evidence of local irritation, and is limited to the part irritated; vide note to page 6, also the following.

"The adhesiveness of the white corpuscles, as of the red ones, is limited to the part irritated. A very good example of this presented itself on one occasion, when a minute drop of chloroform was applied to a small part of a healthy web, so as to induce full dilatation of the arteries and great excess of corpuscles without absolute stagnation. It happened that the part affected was supplied with blood from the branches coming from one side of a principal artery, the main trunk being seated just above the limit between the irritated area and the healthy region, the adjacent part of which received supply from the branches of the vessel on the other side. The latter showed no appearance of adhering white corpuscles, nor did the capillaries which were fed by them; but those of the irritated part, though springing from the same trunk, were remarkably encrusted with them, from their origin to their minutest ramifications within the area, while the capillaries and veins in the same part were similarly affected. This striking appearance continued for hours after the chloroform had been applied. Thus the affection of the white corpuscles of the blood in an irritated part is in all respects strictly parallel to that of the red discs, while the greater adhesiveness of which the former are capable, renders the facts regarding them more obvious and unmistakable."—"Early Stages of Inflammation," page 671.

In the face of facts such as these, it would appear that local irritation and corpuscular adhesiveness are related to each other as cause and effect, and that when the latter is seen to exist, the former may be safely inferred; if this be so, we are justified, in every case of corpuscular extrusion, in affirming the co-existence of irritative or inflammatory action.

(6) In tadpoles which were kept in tanks on artificial diet, and which were debilitated and affected with parasites, the author considers he has observed the occurrence of migration of both red and white cells, in the absence of local inflammation.

In a paper read to the Pathological Society of London, April 21st, 1868, Dr. H. Charlton Bastian gives an excellent *resumé* of the opinions entertained as to the mechanism of cell extrusion by foreign observers, to which he appends the results of his own inquiries. I shall take the liberty of transcribing a few passages of this valuable paper.

"Cohnheim himself adopts the view propounded by Oedmansen, that the capillaries are formed by the juxtaposition of a number of flat epithelial cells, in the angles of union of which certain stomata exist, through which as he thinks the corpuscles are forced by reason of the increased pressure in the vessels, and favoured by the transverse position previously assumed by the corpuscles themselves. This view as to the structure of the capillaries is based upon the appearances presented by these vessels after staining with a weak solution of nitrate of silver, when the ordinary brown lines are said to be produced, such as exist in pavement epithelium in other situations.

"Stricker, who has made careful observations on the genesis and structure of the capillaries, rejects *in toto* this theory, and maintains that their formation by the juxtaposition of epithelial cells is directly negatived by observations he has himself made upon the subject. He believes them to be composed of a yielding, homogeneous protoplasma of a contractile character, and which, in harmony with the properties of this substance, generally has the power of developing processes or outgrowths.

"These, Stricker says he has seen developed from the walls of the capillaries, and he maintains that they subsequently become channelled, and unite with other similar processes, so as to form new capillaries. His explanation, and also Prussak's, of this passage of the red blood corpuscles is, not that they are forced though certain pre-existing pores in the capillary walls, but that they pass out by virtue of some 'active condition' of the capillary wall itself."*

* Assuming that some peculiar condition of the capillary wall exists equivalent to what Stricker designates "an active condition," it is quite certain, from the observation made by Dr. Waller of the corpuscles behaving in the same way after death, that this condition has nothing to do with the capillary wall as a vital structure.

Dr. Bastian disagrees with both these explanations, and is of opinion "that the corpuscles pass out in all these conditions, whether in inflammation, in the artificial scorbutic state, or in mechanical congestion,* by virtue of certain active amœboid movements to which the red corpuscles have been excited, owing to alterations in the nature of the blood plasma having an irritating effect upon them; in fact, that they effect their outward passage by dint of amœboid movements such as the white blood corpuscle has been long known to exhibit."

Dr. Bastian says he was led to adopt this view by watching the phenomena of inflammation in the frog's foot; he found "that in certain capillaries beyond the region where this process existed in its greatest intensity, and in capillaries through which the blood was still flowing, certain red corpuscles seemed occasionally to linger by the side of the capillary, applying their flat surfaces against its walls. Sometimes these were swept away by the blood stream passing over them, and occasionally, before they were completely separated from the capillary wall, I have seen them adhering to this for a moment or two by means of a small thread-like process, as though adhesion to some portion of the capillary wall had taken place, which had only been overcome by the blood stream after the drawing out of a tag-like projection from the yielding substance of the corpuscle. Other corpuscles, which had applied themselves to the capillary wall in the manner above described, were not swept away, and in the space of about fifteen or twenty minutes a distinct projection of the corpuscle was to be seen on the outer side of the capillary wall, which went on increasing till the whole of the corpuscle was within the tissue outside the vessel. This taking place while corpuscles and blood plasma were still freely circulating through the capillary."

In repeating Cohnheim's experiment on mechanical congestion, Dr. Bastian affirms that he has "almost invariably seen that the first corpuscles which penetrate the walls of the capillaries are, not those situated in the vessels which have undergone complete stasis and have become fused together, but rather those contained in capillaries in which an oscillation of blood plasma and corpuscles is still taking place. Here also individual corpuscles apply themselves to the capillary wall by one of their surfaces, and after a time the process of perforation takes place.

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* Vide notes, pages 6-9.

"Occasionally, considerable numbers of corpuscles pass out in this way from capillaries in which no stasis has taken place, and that, too, somewhat earlier than the similar exodus of corpuscles from the capillaries in which complete stasis has occurred.

"From the fact that the corpuscles pass out indifferently at all parts of the wall of the capillary, and with no approach to anything like a regular arrangement, such as one might expect to occur if they were protruded through pre-existing stomata at the junctions of epithelial cells; and because the increased tension in the vessels seems adequate to account for the passage outward of fluids from them, but not of corpuscles contained in this fluid; and, lastly, because the mode in which the corpuscles are seen to become applied by their flat surfaces to the capillary wall is the very reverse of that indicated by Cohnheim as the favourable position which the corpuscles assume for forcible extrusion through pre-existing pores," Dr. Bastian concludes that Cohnheim's explanation of the phenomena is wholly untenable, and falls back upon the amœboid hypothesis.

He considers that "the corpuscle effects its adhesion to the wall of the capillary by throwing out a small amœboid projection, which tends to adhere to, and commence the perforation of, the elastic and yielding capillary walls. This view being supported also by the irregular shape and frequent constrictions of the portion of the corpuscle outside the vessel when more than half of it has passed through the capillary wall." *

Dr. Caton rejects altogether the amœboid hypothesis of Cohnheim and Bastian, and relies entirely on the two conditions of adhesion and congestion. Regarding it as essential that the cell shall be in adhesive contact with the wall of the vessel, he says,

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* These tag or tail-like processes afford no evidence whatever of amœboid movement; they are not protrusions from the corpuscle, but extensions of it, owing to its being adherent at one point or part to the vessel wall. The phenomenon is by no means peculiar to the blood corpuscle, but, as I have before pointed out, may be seen in connection with small masses of liquids submerged in dissimilar liquids. "Again, if a small quantity of chloroform or bisulphuret of carbon be poured into water, the greater portion will sink to the bottom of the water in globules of various sizes. These globules frequently adhere to the flat bottom of the vessel, and on an attempt being made to move them (by shaking the liquid) tail-like appendages are produced."—On "The Causes of various Phenomena of Attraction and Adhesion, as exhibited in Solid Bodies, Films, Vesicles, Liquid Globules, and Blood Corpuscles," Proceedings Royal Society, 1862.

"It seems probable that the occurrence of migration depends on two factors, viz., (1) the degree of pressure in the vessels produced by congestion, and (2) the power of resistance possessed by the walls of the vessels."

Professor Beale leans to the idea that the corpuscles escape through minute ruptures in the walls of the vessels. "Every one," he says, "who has made many minute injections is familiar with the fact that minute longitudinal rents or fissures may be made quite wide enough for a red blood corpuscle to pass through edgeways." Again, "We have a right to ask what leads the white corpuscles to move through the walls of the vessels, if no rents or fissures are made by the preceding over-distension? What determines the selection of the seat of passage? Surely to account for this we must conjure to our assistance some mysterious nerve or other agency. It would be hardly wise to maintain that the corpuscle has the will and wisdom to choose the way as well as the power to move; notwithstanding, the distinguished Virchow himself has not hesitated to accredit epithelial cells with most marvellous attributes, even of desiring to assist friendly epithelial cells in distress." *

If, now, we review the various theories which have been propounded to explain the mechanism of cell extrusion, we shall find that they are all open to very grave objections.

In the first place, the view of Cohnheim labours under the serious disability of attributing the same effect to two markedly distinct causes having nothing in common, a fact that invariably creates a *prima facie* suspicion of incorrectness. Is it at all probable that two distinct causes should be in operation in the extrusion of these corpuscles? Dr. Bastian, alive to this weak point, has endeavoured to bring both the white and red corpuscles under the same law, by assuming that the red corpuscles under irritation become endowed with amœboid powers, or that red corpuscles normally possess vital amœboid capacities, which they can only exhibit under abnormal conditions of the liquor sanguinis, which is supposed to provoke them into activity by its irritating properties.

Against this view it may be urged, that the red corpuscles have never been seen to exhibit any movements which could be with certainty referred to the amœboid class, and secondly, that it is most

* "Medical Times and Gazette," May 9th, 1868.

improbable, in the case of either the red or the white, that the soft plastic structure of the corpuscle should be capable of drilling or perforating the capillary wall, since it cannot for a moment be held that the capillary wall is less resistant than the substance of the corpuscle.

Speaking of Stricker's supposition that the corpuscles are passed through by virtue of some "active" condition of the capillary wall, Dr. Bastian says, "I have been able to observe nothing either for or against it; it seems a pure hypothesis, with not much to be said in its favour." It must be admitted that this statement of Stricker's is exceedingly vague, but I am by no means prepared to agree with Dr. Bastian that it is a pure hypothesis, for I can conceive that Stricker may have observed certain appearances which, although unable to explain, nevertheless gave rise to this idea. The probability of this will, I think, become more apparent when the view I have to propound is before the reader.*

Dr. Caton, as before stated, ignores altogether the amœboid hypothesis, and refers the outward passage of both kinds of corpuscles to the pressure from within induced by congestion.

Dr. Beale's suggestion that the corpuscles escape through minute rents in the capillaries, is opposed to the experience of all observers, who, from Waller downward, universally concur in the opinion that no permanent apertures of exit remain, and so great is the number of the extruded corpuscles in some cases, that it would be necessary to consider the vessels as ruptured all over.

It will be seen, then, that these hypotheses fall short in one important particular, inasmuch as they afford no explanation whatever of by far the most singular part of the process, viz., the fact that the apertures through which the corpuscles pass, again close up and become invisible. The question indeed is, not so much how the corpuscles get out, as how they get out without leaving any permanent trace of the apertures through which they have so recently passed, and which were so palpable during the period of transit.

Before proceeding to elaborate my own views, it may be well to re-state succinctly the various points upon which observers are agreed.

(1) Both white and red corpuscles pass out of the vessels through apertures which can neither be seen before their ingress

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* Vide notes, pages 4 and 10.

into, or egress from, the vessel wall, but only during the period of transit.

(2) An essential and primary step in the process is, that the corpuscles shall adhere, or more properly cohere, to the wall of the vessel.

(3) These cohering corpuscles are subsequently subjected to pressure from within.

With these conditions fully before our minds, we will proceed to enquire if in physics we can find the analogue of these seemingly mysterious phenomena.

PHYSICAL PRINCIPLES CONCERNED IN EXTRUSION OF THE CORPUSCULAR ELEMENTS.

In the first place, this phenomenon of the passage of bodies through films or membranes is by no means confined to the capillary walls, the same thing having been observed in connection with nucleated blood corpuscles, such, for example, as those of the frog. In these cases no rupture or aperture of exit has been discovered.

It is obvious that the escape of the nucleus from its capsule without rupture, and the passage of the entire blood corpuscle through the capillary wall without rupture, are phenomena of the same class, and the explanation which will suffice to clear up the one will also apply with equal force to the other.

As a matter of fact, it will be admitted that we can form no *a priori* conception of one form-retaining body passing through another without either rupturing it, or distending certain holes or pores which it may already possess. This, however, is just one of those cases in which conceivability is no test whatever of possibility.

To comprehend these phenomena it is necessary to bear in mind the ultimate constitution of those animal membranes which form alike the capsules of the corpuscles and the parietes of the capillaries. All the membranes which enter into the animal body may be divided into two orders—(*a*) the very fine, structureless, homogeneous films, which must be regarded as simple cohesion-membranes, in contradistinction to the second order of (*b*) coarser membranes, to which certain mechanical arrangements are superadded, which have the effect of increasing their strength, such, for example, as structure, the result of interlacing fibres. In

films of collodion, gelatine, albumen, india rubber, soap, we have examples of the first class of membranes.

It is with this class that we are now concerned, and these are susceptible of two states, the fixed or rigid condition, and the contractile or elastic colloidal state dependent upon the presence of the principle of "flow," which principle may be operative in every shade and degree, from perfect liquidity to absolute rigidity.

It will be sufficient to state here that the more colloid and plastic these membranes are, or, in other words, the more they approximate in their constitution to liquids, so do they proportionately cease to obey exclusively the laws of rigid bodies, and begin to exhibit intermediate properties or qualities, some of which belong to solids and others to liquids.

We may take the soap film as the best illustration we can find, on a large scale, of the class of homogeneous cohesion films possessing in the greatest perfection this principle of "flow," and as exhibiting to the fullest extent phenomena which I have generalized under the term, "Progressive cohesive attraction."

By the study of the soap-film we may acquire a knowledge of many of the laws which are operative in connection with delicate colloidal films in general.*

The steps, for example, in the production of an ordinary soap-sphere are very remarkable, as exemplifying the power which these films possess, under the influence of progressive cohesion, to perfect any absence of continuity which may exist in their structure.

The first essential in the process of forming a soap-sphere is the production, upon the mouth of the pipe-bowl, of a film stretching evenly across from every point of the circumference. The production of this film is a far more complex operation than is generally supposed.

If for the pipe-bowl we substitute a ring, having a diameter of from twelve to eighteen inches, we are enabled to watch, as the process proceeds, the manner in which the film is formed.

Having submerged the ring in a solution of soap, we observe, as we gradually raise it out, that its circumference brings up from the

* All the experiments about to be detailed may readily be performed on a smaller scale on films and structures formed from such colloid substances as albumen, globulin, gelatine, &c., both in the soluble and in the isomeric or pectous condition.

liquid a band-like film of a cylindrical or tubular form, which is attached to the ring above and the liquid below; raising up the ring still higher we find that this annular film contracts in diameter at every part except at its attachment to the circumference of the ring, which is of course fixed. This quality of the film to contract between opposing points of extension causes it to take on the shape of an inverted cone with curved sides, the convexities of which are directed inward. The tendency to assume the inverted cone shape is further assisted by the fact, that the film in contracting travels inward upon the surface of the solution towards a central point, so that from the ring downward to the surface of the solution the diameter of the tubular film is continually decreasing. The shortest diameter is not, however, immediately upon the surface of the liquid, but at a little distance from it, and consequently, as the contraction proceeds, it will be at this spot that the union of the sides of the film and the separation will take place. This arises from the fact that this is the weakest point of tension between the ring and the liquid, and therefore the one in which circumferential contraction can take place with the greatest ease and effect. Thus we see that the tubular film which we have raised really becomes constricted into two portions, an upper portion which immediately contracts into a plane surface upon the ring, and a smaller and lower portion, which, in consequence of including air, becomes a hemisphere, and remains attached to the surface of the solution. (Vide figs. 1, 2, 3, Plate I.)

If having formed such a film upon a ring or pipe-bowl, we proceed to blow down upon it, we distend it into a sphere, but it is obvious that until the sphere is detached there exists a free opening into it at its upper part, which becomes suddenly sealed up by cohesion of the sides of the film, at the moment preceding detachment. The manner in which continuity is effected in the case of the soap-sphere is illustrated in Plate II., figs. 1, 2, 3, and is seen to be a repetition of what takes place in the formation of the primary film.*

In the production, therefore, of the ordinary soap-sphere, we have no less than four examples of the maintenance of continuity

* In order that the manner in which the sphere becomes sealed up should be better observed, it has been allowed to cohere to a film previously formed upon the ring, then by slowly increasing the distance between the film and the ring the severance can be gradually effected, and the process of division into two air-enclosing cavities watched as it proceeds.

where rupture might have been *a priori* anticipated, two in the production of the film, and two in the sealing up of the sphere.

The next point to which I will draw attention is the power possessed by these films to repair breaches of continuity that may be made in them subsequently to their formation. If any rigid body be wetted, it is quite possible to thrust it through one of these films, move it about, and again withdraw it without interfering with the integrity of the structure. In fig. 1, Plate III., a smooth, bulbous rod of glass is represented as thrust through the film; it is not, however, essential that the body should be either smooth or regular, for the same may be done with the naked fist and arm, as in fig. 2, Plate III.

I have demonstrated elsewhere that the blood corpuscles undergo a mode of aggregation in obedience to progressive mutual attraction, in precisely the same fashion as soap spheres, *i.e.* if they touch at any one point they gradually, by the operation of double cohesion, convert each other into polyhedral shaped bodies.* (Vide Plate IV., figs. 1 and 2.)

If we take any smooth rigid surface and allow any point in the circumference of a bubble to impinge against it, we find that it becomes so drawn down to the plate in every direction from this point as a centre as to take on a hemispherical form. (Vide Plate IV., fig. 3.)

But if for the rigid surface we substitute a delicate plastic film, such as the soap film, and allow the bubble to come in contact with it at one point, taking care that there is a free supply of liquid upon its exterior at this point, we observe that the result is different. In this case the soap-sphere takes on the form of two watch-glasses in apposition at their edges, one of the curves being present on each side of the film. The soap-sphere has in fact penetrated the film and arranged itself so that half is on one side and half on the other. (Vide fig. 1, Plate V.)

Now this is precisely analogous to what takes place with the capillary when the corpuscle has entered into cohesion with its wall, " a protuberance is seen on the outer surface."

If we can subject this soap-sphere to pressure on one side only, we shall cause it to protrude through the film still further; this we can do by forming one sphere within another. This inner sphere,

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* Proceedings Royal Society, May 1869.

it will be observed, protrudes more than in the case of the simple film. (Vide Plate IV., fig. 3.)

That there is pressure within a bubble may be known by the fact, that, if left with an aperture in it, it will gradually force out the contained air, and become again a simple film by its strong cohesive tendency.

Further, it will be seen that we can with the greatest ease separate these cohering spheres, and bring them bodily through the film without injury to the one or the other, this is a parallel case to the passage of the nucleus through the capsule of the corpuscle, and of the corpuscle itself through the capillary wall. (Vide figs. 1 and 2, Plate V.)

I have previously shown that the corpuscles are among themselves amenable to the same laws as the soap-spheres, and we have only to infer that they bear the same relation to the capillary walls as these spheres and films bear to each other. The margin of speculation is therefore small. (Vide Plate IV., figs. 1 and 2.)

In the case of the corpuscles, this relation is of course only seen under abnormal conditions, simply because it is a physical law, which, in the normal working of the animal economy, requires to be antagonised.

It must also be observed that it is only under certain conditions that the soap-spheres attract each other, or are attracted by rigid surfaces or plastic films. This occurs only when free liquid is cohering to their surfaces. If before bringing them into contact we allow the soap-film and sphere to become moderately dry, they will not attract each other, but the former will support the latter as a perfect sphere, instead of drawing it down by progressive cohesion, and arranging it half-way through itself as shown in fig. 1, Plate V. Compare with fig. 3, Plate IV.

Just so with the corpuscles; they do not unite either with each other or with the capillary wall, unless their normal osmotic relations are disturbed, the exosmotic current setting in excessively, when their external surfaces become coated with content matter, and they become instantly attractive of the capillary wall or glass slide as the case may be.

Suppose, for example, a number of easily moveable bodies, such as cork discs, to be submerged in water, they are neither attractive of each other, nor of the smooth sides of the vessel in which they may be. Both their exteriors and the sides of the vessel are wetted by one and the same liquid, viz., the water, and there is everywhere

a cohesive equilibrium. Precisely the same relation obtains between the blood corpuscles and the capillary walls in a state of health; they are wetted by and surrounded on all sides by liquor sanguinis, and cohesive equilibrium prevails, a condition practically equivalent to the absence of cohesion altogether. If we modify our experiment by first wetting the cork discs with some liquid which is either (as to cohesion) neutral or antagonistic to water—in other words, not miscible or only imperfectly miscible with it—we destroy the cohesive equilibrium, and the discs cohere to one another and to the sides of the containing vessel. In the case of the corpuscles, the second liquid essential for the production of cohesive inequilibrium exudes by osmosis from their interior, and so soon as it appears upon their exterior, they must cohere to each other and to the capillary wall.

The corpuscles having cohered to the capillary wall, their ease of transmission through this structure is simply a question of the extent to which it possesses "the principle of flow" under the pressure to which it is subjected.

In our experiments conducted in the atmosphere, the bodies may be regarded as surrounded by a neutral medium, and therefore when free liquid is present, we have the necessary condition of cohesive inequilibrium.

In the paper before referred to, "On the Laws concerned in the Aggregation of the Blood Corpuscles," I have given numerous examples of the operation of progressive cohesive attraction, but in this place I wish to call attention to the demonstration there given of its relation to plane surfaces, and to that end introduce the following quotation:—"In thinking over the probable relations which delicate and plastic films might bear to each other, I was again helped out by the recollection of an observation made some years previously upon fine films of collodion. It was found that if one of these films, while still in the wet condition, was detached from the glass plate upon which it had been formed, it immediately, in opposition to gravity, sprang back to its former situation into contact with the glass plate, precisely as if it were electric. This phenomenon of attraction may be witnessed in a somewhat less energetic degree by simply spreading upon a glass plate a thoroughly wetted piece of thin cambric paper, taking care that the contact is perfect throughout. On separating the paper from the glass to nearly its whole extent, and allowing it to hang down at a right angle from the plate, which is held in the horizontal position, it

will be found to gradually raise itself upwards, and reassume its old position of contact with the surface of the glass plate." (Vide fig. 1, Plate VI.)

Taking this experiment as a starting point, we will extend the consideration to surfaces of a different character. In the first place, we find that this law continues to operate with great facility in connection with surfaces curved in one direction only, whether the surface used be convex or concave, in both cases the film of paper or collodion applies itself evenly to the surface in the gradual progressive manner before explained.

If, however, for surfaces curved in one direction only we substitute such as are curved in all directions, for example, the outer or convex, or the inner or concave surface of a hollow sphere, we find ourselves confronted with a new set of difficulties; out of which we may evolve the statement, that, for any film to apply itself evenly and regularly to either the convex or concave surface of a sphere under the influence of progressive attraction, it is necessary that the film should be, in several particulars of its constitution, very different from the class of films by means of which we have been able to perform the three preceding experiments.

If, by way of illustration, we apply a film of wetted collodion or fine cambric paper to the sphere, so that one point of the convexity of the latter may come in contact with the centre of the film, the attraction will only succeed in pulling it down to the surface of the sphere at certain points, the intermediate puckered parts not being in contact, and by no possibility can they become applied. From this we see that for the film to be laid down evenly it would be necessary that it should contract in certain parts, that in fact the puckered or surplus material should be taken up. We may say then that any film which can adapt itself to the surface of a spherical body must possess the two-fold quality of facile contraction and expansion, these qualities being controlled in their operation by progressive cohesive attraction. Such a film must be a simple, colloidal, cohesion-membrane in possession of the property of "flow."

If, further, we apply to a sphere a film known to possess facile properties of expansion and contraction under the influence of slight forces, such as progressive cohesive attraction, the first thing seen to occur is cohesion of the film to the sphere at the point of contact, and from this point, as a centre of operation, the film proceeds to apply itself gradually in all directions, so that the sphere becomes coated or covered evenly by it. And this process goes

on until the attraction becomes balanced or fully antagonised by the elasticity of the film, *i.e.* the attraction is only powerful enough to stretch the film to a certain extent, so that if the rigid object be fixed, as is the case with the glass bulb when held immovably, we get a disposition of the film, such as is represented in fig. 4, Plate VII. In other words, a sufficient degree of attachment of the film to the bulb has taken place to stretch the film backward out of its normal plane. If now we push the bulb farther forward, the film still continues to apply itself to its surface, and having reached the equatorial line of the sphere, descends on the opposite hemisphere till the bulb is completely coated. But it will be said the bulb does not then really produce an infraction of the film, but merely attracts it down to its surface, and in so doing stretches it, so that it is in reality a new conformation of the film, and not a breach of its continuity. That this is true to a certain extent there is no doubt, but it is not all the truth, for we may wipe the bulb dry after it has passed through the film without interfering with the continuity of the latter. All that appears to be necessary for these effects to display themselves is, that there should be mutual cohesion between the film and the body passing through it; for if we press against one of these delicate films with a substance which has no cohesion for it, *e.g.* a current of air or a dry soap-sphere, it simply distends the film, neither bursting it nor giving rise to an aperture in it; while in the case of a body to which the film can cohere, it would appear to be easier for the latter to allow the passage of the cohering body than to suffer distension by it, and this because it has under these conditions as great an attraction for the particles of the body as for its own particles. When the cohering body has become perfectly applied to the film, the latter, by the cohesiveness of its own particles, contracts to the greatest degree possible consistent with still maintaining its attachment to the cohering body, and this in spherical shaped bodies leads to a condition of things in which half the body is within and half without the film or wall; * therefore the rest of the process must be accomplished by pressure from within. It is easy to see that the manner or degree

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* In Plate III., fig. 3, an excellent illustration of this principle is afforded. A light India-rubber ball or balloon is suspended from a fixed point *a*, its surface having been previously wetted over with a solution of soap. When a soap-film formed upon the ring, as in the previous experiments,

in which the corpuscle or body adheres to the film will determine very materially the method of its transmission. All then that is essential for a rigid or a plastic body to pass through a colloid film is, (1) an intimate power of cohesion either mediately or immediately between the film and the body; (2) a certain amount of pressure from within; (3) power in the substance of the film to cohere to the surface of the body, or to some intermediate matter which already coheres to its surface, during its passage; (4) cohesive plasticity of the particles of the material of which the film itself is formed, so that the breach in it may become reunited as it descends upon the opposite surface of the body which is being extruded.

It is quite remarkable to how great an extent these conditions appear to be complied with in the passage of the corpuscle through the capillary wall, as affirmed by independent observers.

In the factitious examples by which I have sought to illustrate these effects, the film moves over the body, or the body through the film, by virtue of the intermediate agency of the solution which has cohesive attraction for both; and the film does not rupture, because, while the body is travelling through, it can continue to cohere until it is brought again into contact with its own particles at the opposite pole of the extruded body.

Theoretically, it should leave the sphere or protruding body as represented in Plate VII., fig. 1, having gradually narrowed the aperture to absolute union at a focal point, or, according to the laying-down view, having re-peeled itself from the bulb. Practically, however, I find that the film rarely leaves the bulb or sphere, without forming on it a small hemispherical bubble, which is large in the ratio of the rapidity with which the detachment is effected. (Vide Plate VII., fig. 3.)

If detached with very great care the bubble is exceedingly small, but I could not succeed with a spherical bulb in getting rid of it altogether. With a more conical bulb, however, this was readily effected. In the case of the sphere, the film is in reality

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is brought into contact with one part of its convexity, the ball is at once drawn into the film as far as its equator, and is compelled to retain this position in opposition to the force of gravity. This is the exact converse of the case of the fixed bulb, in which the attraction is satisfied at the expense of the extensibility of the film.

drawn out into a little neck, as in the other examples in which continuity is effected, and this neck being pulled into two, and both parts cohering at the point of severance, we get on the one side the perfected film, and on the other a small enclosure of air which takes on the hemispherical form. This is owing to the annular contraction of the tubular part. If the body were small, or less spherical, or the film a trifle more rigid, this would not occur. (Vide Plate VII., fig. 2.)

I find in fact by experiment that smaller bodies, more conical in their termination, will not do this, but draw out a kind of streak of solution as they leave the film; a fact I have often observed with the white corpuscles. In this case the film is brought to a focus upon the body, and not at a slight distance from it, so that either or both these modes might obtain with the corpuscle. In some cases the streak of solution is absent. The method of sealing which leaves behind a portion of the film is probably a necessity of every case of repair of continuity, with the exception of that of transmission of a foreign body through a film.

In the case of the blood corpuscle it would not appear that the capillary wall became applied over the surface of the corpuscle to any great extent, but that, having effected cohesion, it becomes easier for the capillary wall to give way and glide over the corpuscle than to be distended by it. And this is effected much more slowly than in the case of the factitious examples which I have given; the content matter of the corpuscle abnormally present upon its surface being, as before stated, the material through the medium of which the cohesion is effected.

THE RELATION OF EXTRUDED BLOOD CORPUSCLES TO PUS AND TO THE SO-CALLED FIBRINOUS EXUDATION OF INFLAMMATION.

The white blood corpuscle, the discovery of which was claimed by Mandl in 1838, but which in truth had been observed at a much earlier period by our countryman Hewson, has always been an anatomical element of great interest both to the physiologist and pathologist. To the former, mainly on account of its assumed progenital relationship to the red corpuscle, and its curious property of exhibiting spontaneous or amœboid movement. To the latter, on account of the singular similitude which it bears to the morphological element of pus, which has been termed the "blood of

pathology." As before seen, the two latter mentioned properties are those which constitute its interest in the present connection.

The analogy between the pale corpuscle and the pus cell is so complete as to render it impossible to differentiate one from the other. When Dr. Hughes Bennett observed his first case of leucocythemia, which we now all know consists in an enormous increase of the colourless corpuscles of the blood, he considered that he had under his eye innumerable pus cells, and was led to designate the affection, "suppuration of the blood without inflammation." It must be borne in mind that the attention of pathologists was much directed toward the subjects of pyæmia and inflammation, and that Addison and Williams had published their conviction that the cause of inflammation was an increase of the colourless corpuscles. Piorry also supposed that the blood itself was capable of becoming inflamed, and that this constituted pyæmia. It is not at all surprising, therefore, that Bennett, under the influence of these views, seeing what he believed to be a multitude of pus cells in the blood without any febrile or inflammatory co-existences or sequences, was induced to characterise the disease in the manner just mentioned. At the same time it must be admitted that he did not entirely overlook the possibility of these cells being the colourless corpuscles of the blood, for he said, "the blood in a state of health contains a number of colourless corpuscles which closely resemble those of pus."

Six weeks after the publication of this case by Bennett, a similar one was observed by Virchow of Berlin, and he gave to the disease the name of Leukæmia, and subsequently that of Leucocytosis.

Bennett has all along affirmed that there is no real difference between the colourless cells which he observed in 1845 in such numbers, and the pus cell; and Virchow, on page 155, "Cellular Pathology," published 1860, says, "A pus corpuscle can be distinguished from a colourless blood cell by nothing else than by its mode of origin. If you do not know whence it has come, you cannot say what it is, you may conceive the greatest doubt whether you are to regard a body of the kind as a pus or a colourless blood corpuscle. In every case of the sort the points to be considered are, where the body belongs to, and where its home is. If this proves to be external to the blood, you may safely conclude that it is pus; but if this is not the case, you have to do with blood cells."

Bennett very strongly, and with good reason, objects to this

definition of Virchow. "According to this definition," he says, "a cell closely resembling a pus cell in the saliva, inasmuch as it originates externally to the blood, is a pus and not a salivary cell. On the other hand, if a blood vessel be full of a thick, creamy, yellow fluid, containing a multitude of cells indistinguishable from pus cells, inasmuch as these are formed in the blood it is not pus. According to Professor Virchow, practical men in future, when they see in a case of puerperal phlebitis, the uterine sinuses and neighbouring veins distended with pus, or surgeons, when they see the veins of the arm full of purulent matter from the bend of the elbow to the axilla, are to conclude that it is not pus. I maintain on the contrary that such fluid is pus, because it results from inflammation; that is the real question to be considered."*

From what has been said it will be seen that Bennett, Virchow, Waller, Cohnheim, and others, regard the white corpuscle as identical with the pus cell; that the two latter would consider it a pus cell if they found it outside the proper blood channels; and that the former (Bennett) would do so only if its presence in a part had been contingent upon inflammation.

I have attempted to show in the early part of this paper that cell extrusion never takes place except under conditions in which the white corpuscles exhibit adhesiveness, and I have further sought to bring out that this adhesiveness is the initial visible sign of inflammation, or of the operation of irritation.†

If this be correct, it will be apparent that while the view of Virchow would not compel him to accept extruded white blood corpuscles as pus-cells, the converse would be true of Bennett, because the very act of extrusion is the result of inflammatory change. The statement of Virchow amounts simply to this:—If you see a body like a white blood cell, and you can make out satisfactorily that it is a derivation of connective tissue or epithelial structure, then you may affirm that it is a pus cell; but if, on the contrary, you can show that it has escaped from the blood, then it is a white blood cell. This is, after all, a question of designations. The real question at issue is, whether, under a certain degree of irritation, numbers of white blood cells can accumulate in the vessels of a part and become extruded through the vessel walls, and in their new habitat, surrounded by exudation fluid, commence a process of

* Vide "Lancet," 1863, p. 380.

† Vide foot-notes, pages 6 and 9.

multiplication, and so constitute some of those swellings which we call abscesses.

That such is the case there seems to be the strongest presumptive evidence, and such a view by no means ignores the possibility that other formations of pus may be due to the proliferation of connective tissue and epithelial cells. Indeed, there is the strongest probability that the *large* white blood corpuscle itself is nothing more than the nucleus derived from the epithelial lining of the lymphatic and vascular tract; and if this prove true, there is not the slightest reason why it should not be regarded as endowed with the properties of epithelial nuclei in general. That is to say, if abnormal conditions (irritation) can excite increased proliferation in connective tissue and epithelial nuclei, it may be expected confidently to do the same in the white blood cell. Bear in mind there is no denying the fact that, in all cases of inflammation, white corpuscles do escape in large numbers from the vessels, and therefore some of the contents of an abscess are undoubtedly such white corpuscles; consequently we must affirm that *some* of the white cells in a common abscess are undoubtedly blood cells.

It remains to refer to one other writer upon this subject, one whose opinion, on account of his vast histological knowledge, is entitled to be received on such a question with the profoundest respect; I allude to Dr. Lionel Beale. He says:—"Cohnheim has discovered the remarkable and interesting fact, that, in the living frog, white corpuscles may be seen to pass through the walls of the blood vessels, and has arrived at the conclusion that the corpuscles in their new situation are pus corpuscles. But it is difficult to understand how, by the mere passage through membrane, so great a change as is supposed can be effected; for a white blood corpuscle is one thing, and a pus corpuscle another. Suppose the pus corpuscle to pass back again into the vessel, does it remain a pus corpuscle, or is it again converted into a white blood corpuscle? But the idea of a true pus corpuscle becoming a white blood corpuscle cannot be entertained. It would be as unreasonable to maintain that it might become a brain cell. It seems to me that in this view there is a confusion of things quite distinct from one another. A pus corpuscle is as far removed from a white blood corpuscle as it is from a healthy epithelial or other cell. If it be said a white blood corpuscle looks like a pus corpuscle, I would answer, 'No two forms of germinal matter, however much they may differ in origin, properties, or

powers, can be distinguished from one another by their microscopical or chemical characters. We could not distinguish the germinal matter of the lowest, simplest living thing from that of the highest brain cell of man. They differ in power and in action, although the material composing the one resembles in appearance that which constitutes the other.' . . . . In all cases true pus corpuscles are the descendants of normal germinal matter, and result from its increase and multiplication at a greater rate than occurs in health. If the living germinal matter of any tissue, or that composing white blood, lymph, or chyle corpuscles, receives an increased supply of pabulum, it will grow, divide, and subdivide, and at a gradually increasing rate if the conditions be favourable. The masses resulting from this process acquire properties and powers very different from those of the originals. Hence, although a white blood corpuscle growing and multiplying under altered conditions may give rise to multitudes of pus corpuscles, nothing can, I think, convert an individual white blood corpuscle into a pus corpuscle, and it is quite certain that under no circumstances whatever can pus corpuscles undergo conversion into, or give origin to, white corpuscles. We might as well proceed to discuss whether a new and highly elaborate structure, with vessels, nerves, and special anatomical elements, could be formed from the contents of an abscess."*

I submit that Professor Beale has mistaken the position of the advocates of this view of pus formation. They maintain that no morphological or chemical difference exists between the white corpuscle and the pus cell, and therefore, so far from affirming that any change in the nature of the cell takes place during the passage through the wall of the capillary, such change would be fatal to their theory. The simple change of place warrants in their estimation the change of name; the designations are in fact convertible. In fine, they affirm that the same anatomical element has been hitherto variously denominated a white blood cell, or a pus cell, according to the locality in which it has chanced to be discovered; and further, had the possibility of the extrusion of the white blood corpuscles into the tissues been known from the beginning, the designation "pus cell" would never have been needed or invented.

It is true that Dr. Beale affirms that there is some essential difference between the white blood corpuscle and the pus cell, but

* "Medical Times and Gazette," May 9th, 1868.

it must be confessed that the evidence in favour of this is not at all satisfactory. He conceives it quite possible for white blood corpuscles, under altered circumstances of nutrition, to give rise to pus corpuscles, but such corpuscles he would regard as degenerated offspring, and therefore quite incapable of reproducing structures in all respects similar to their original progenitors. Thus he assumes a difference, and at the same time admits the impossibility of demonstrating its existence; for if we can find no morphological or chemical difference, and are compelled to take as our guide "the differences in power and action" which distinguish various other indistinguishable forms of germinal matter, what shall we find? Why, that waiving the dubious doctrine of the origin of the red corpuscle from the white, no property or power can with certainty be ascribed to the white blood cell, but which is as certainly predicable of the pus cell.

(1) As anatomical elements they offer no points of distinction.

(2) Their chemistry is the same.

(3) Both possess amœboid powers.

(4) To both is accorded the property of growth and multiplication by subdivision.

(5) Neither of them contribute to the formation of any higher structure.

(6) Neither of them eventuate in anything different from cells, or as Beale would say, masses of germinal matter, but as such live, die, and disintegrate.

If any evidence were needed that tissues possess within themselves their own life properties and powers, no better exemplification of the fact could be found than in the recent success which has attended the transplantation of minute detached portions of skin. It is quite clear that the conglomerate tissues which form these little pieces of skin possess the property directly to absorb from the surfaces upon which they are placed the elements of their nutrition, and to convert them into their like.

It is now some years ago since Virchow urged the importance of recognising the fact, that the individual elements of tissues, when incited by a stimulus directly applied to them, had the power of taking up an increased quantity of material quite independently of any vascular or nervous change. These views that learned pathologist enforced by examples derived from articular cartilage and the cornea. He showed that if a thread were passed through a cartilage, the primary visible effect was an enlargement of the cells around

the thread and in its tract, whilst the more remote cells remained unaffected. A condition was thus induced which, as the result of irritation, according to this author, could not be distinguished from simple hypertrophy, and this brought about those modern ideas of inflammation which may be briefly expressed thus:—"The direct irritation of tissue elements leads in the first place to increased absorption and consequent enlargement of these elements, and subsequently to heterologous proliferation of the nuclei in the shape of pus." Any changes which may occur in the blood or vessels are regarded as entirely secondary and subordinate. In this way those important changes in the blood, such as stasis and exudation, have been reduced to so subordinate a position that it is almost the fashion now-a-days to ignore them altogether. Against this tendency, I think, a stand requires to be made. These teachings of the great pathologist embody but a portion of the truth, and are incompetent to the explanation of the phenomena of inflammation as they occur in compound tissues and organs, in which the effects of direct irritation are various and complex, and re-act upon each other in the production of still more complex results. Space will not permit me to state my views upon this question, save in the most epitomised form, and I will therefore embody them in a series of propositions.

(1) It must be admitted that every tissue of the organism possesses, as an inherent quality, the power to absorb such material as it requires for its growth.

(2) This nutritive material is absorbed in the shape of solution of organic materials supplied by the blood.

(3) This capacity of the tissues to absorb liquid matter in their vicinity involves a constant supply, which is emitted laterally by the blood vessels, and which fills up the capillary interstices of the tissues. This may be called the normal exudation stream, the motive force of which is the growing and developing tissue.

(4) When, as a sequence of direct irritation, the tissue elements absorb more freely than *usual* the liquid in which they are bathed, the result is that the normal exudation stream is increased in its rate of flow, until a balance is attained between the power of the tissue elements to absorb on the one hand, and the capacity for lateral exudation in the vessels on the other. That is to say, a mean is attained between demand and supply.

(5) These simple principles hold good in all nerveless and non-vascular structures, such as the cornea and cartilage, but the case is

utterly different when a part irritated contains, in addition to the simpler ordinary tissue elements, blood vessels and nerves, for these structures are simultaneously subjected to irritation, and you get superadded to the effects which flow from simple cell-tissue irritation, such results as irritation may be capable of effecting directly or indirectly in the tissue elements of and in the functions of blood vessels, blood corpuscles, blood plasma, and nerves, together with their sequences.

Let us take for example a tract of the skin—one of the first results of irritation of such a compound structure is pain ; *ergo*, sensory nerve elements have been excited. Simultaneously we get momentary pallor, succeeded by increased redness. Microscopic investigation of transparent parts teaches us that this pallor corresponds to contraction of the blood vessels, and the increased redness to dilatation of the same, the result of vaso-motor fatigue, or, in cases of excessive irritation, paralysis. If the irritation is very severe, we may get in addition intrinsic muscular paralysis.* Here we have the function of two important tissues thrown into abeyance.

(6) In the case of the skin we have also direct irritation of connective tissue elements, leading to increased absorption of liquid in the vicinity, and therefore to an increase of the normal exudation stream, which is now no longer, as in the case of the cartilage, antagonised by the normal contraction of distant blood vessels. It is this increased normal exudation stream which I have designated the "primary exudation." The extent or rate of the primary exudation will determine the several sequences which may occur.

If but little over the normal nutritive ratio, there will be but little inspissation of the liquor sanguinis, the first visible result of this being the display of adhesiveness in the white corpuscles; and if the irritation is not unduly severe, and the primary exudation consequently moderate, the vessels will become lined and even filled with white corpuscles, and a condition attained which, when displayed in greatest perfection, may be designated "white stasis." For the production of this form of stasis, a degree of irritation just short of that which induces cohesiveness of the red corpuscles is necessary, because it depends upon the white corpuscles becom-

* Muscular tissue appears to be capable of maintaining, even in the absence of nerve, a certain degree of *tone*.

ing cohesive, while the red are as yet scarcely affected in this respect; so that practically the white corpuscles become filtered out from the red, and left behind in the vessels by virtue of their tendency to adhere to one another and to the vessel walls. It is therefore in long continued irritation of an intensity insufficient to induce cohesiveness of the red corpuscles that we get greatest extrusion of the white blood cells, and consequently in which we should be likely to get formation of pus in this manner to the greatest extent.

On the other hand, if the irritation is more severe, and the primary or lateral exudation correspondingly excessive, the vessels are robbed of their liquid matter at a greater rate than it is supplied. Red corpuscles lag behind and numerically increase. At the same time, when the inspissation attains a given degree, they become cohesive, blend together, block up the vessels, and exhibit the condition which, in contradistinction to the former kind, may be designated "red stasis." It is at this juncture when stasis (white or red) has occurred, that the secondary exudation comes into existence as the result of pressure. The course of the blood being arrested, there is nothing left save for its liquid portions to stream out laterally, while the pressure exerted on the blocked portions drives through the walls of the capillaries the red or white corpuscular matter as the case may be. (Vide Plate VIII., figs. 1 and 2.)

This extruded corpuscular matter being fibrino-plastic in its character, unites with the fibrinogen of the liquor sanguinis simultaneously exuded, and forms upon the walls of the vessels and contiguous parts that inflammatory product so long recognised as the coagulable lymph of Hunter, but erroneously regarded as a fibrinous exudation from the blood. While it is quite true that this product is fibrine, there is no proof that it ever existed as such in the blood; on the contrary, there is the strongest evidence that it is formed at the period when the corpuscular matter is forced in such quantities through the walls of the vascular parietes during the condition of stasis.

This view is in accordance with the recent researches of Professor Heynsius, which demonstrate that the great bulk of the substance known as fibrine is derived from the content matter of the corpuscles (fibrino-plastin).

These facts taken together furnish us at once with an explanation of the source of the fibrinous deposits which result from in-

flammatory action. The tint of the exuded lymph is well known to be very variable, and this is accounted for by the varying amount of cruorin present. If the form of stasis which obtains be due to the blocking up of the vessels with white cells, the globulin extruded will give rise to a pure white form of coagulable lymph. If, on the contrary, red stasis prevails, the lymph will be of a reddish colour, and between these extremes we may have yellow green, or in fact any shade of colour capable of being imparted by cruorin in a dilute or concentrated state, so that the colour of the lymph, being dependent on the mixed character of the stasis, is really an indication of the intensity of the irritation which has existed.

PLATE I.

FIG. 1

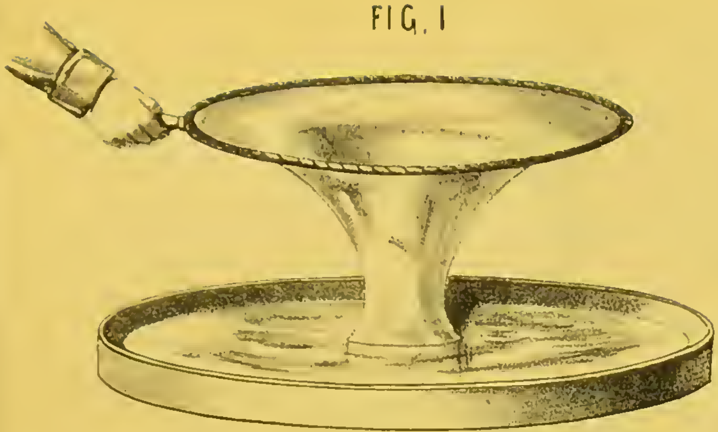

FIG. 2

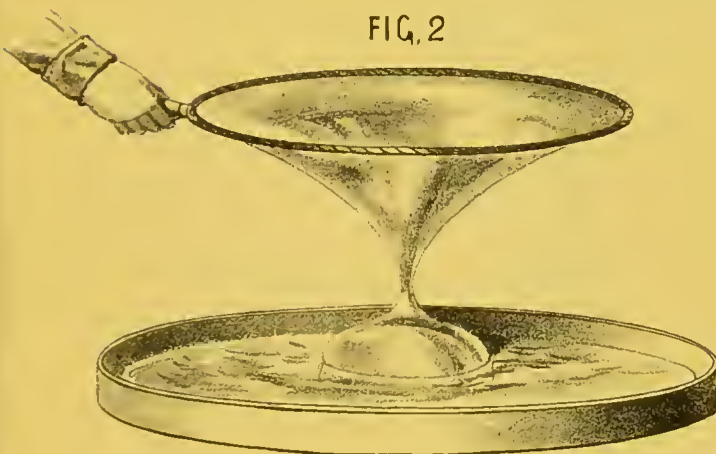

FIG. 3

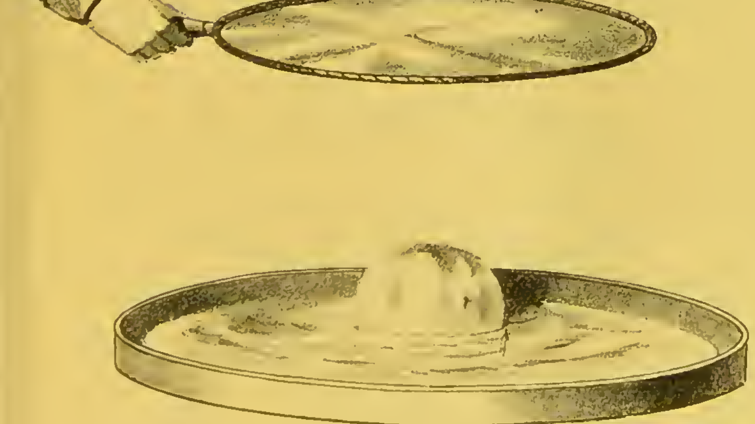

FIG. 1

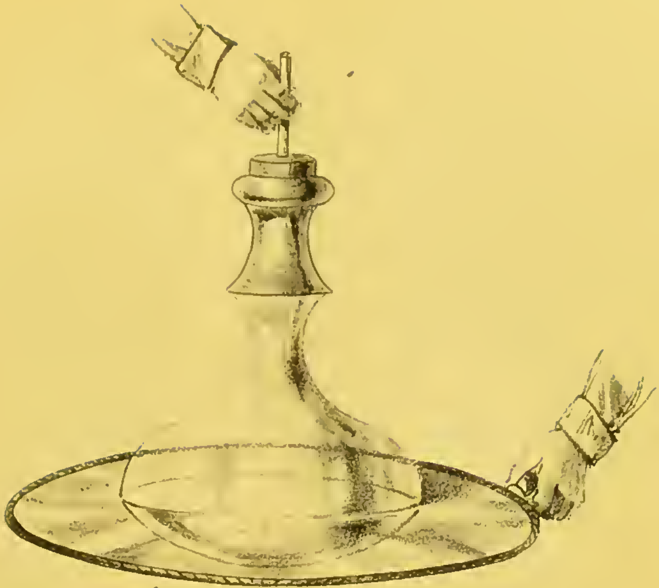

FIG. 2.

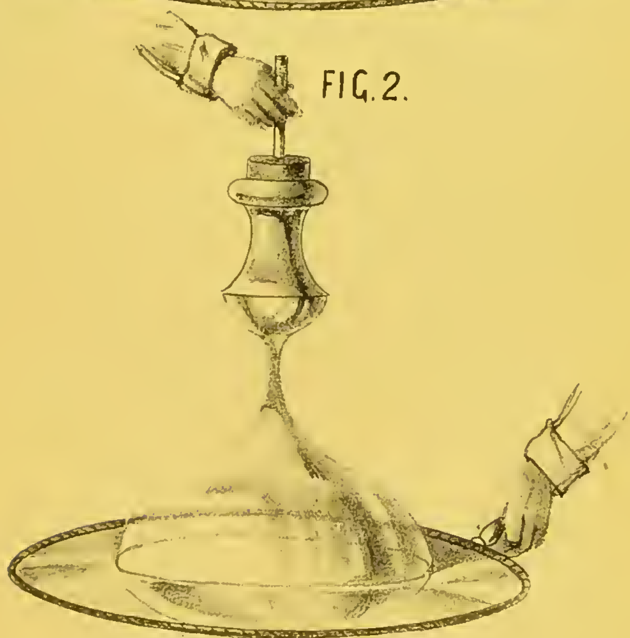

FIG. 3.

FIG. 1.

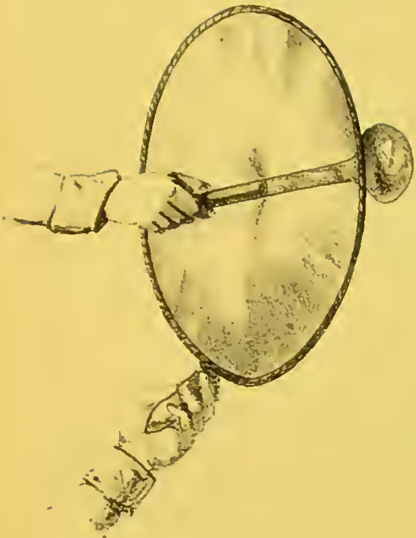

FIG. 2.

FIG 3.

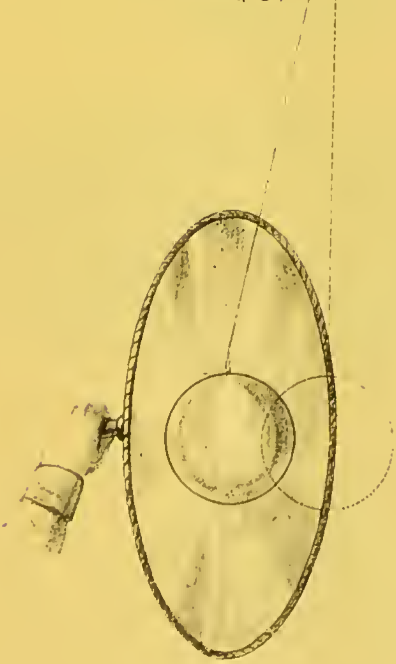

FIG. 1.

Minute Soap Bubbles

FIG. 2

Blood Corpuscles

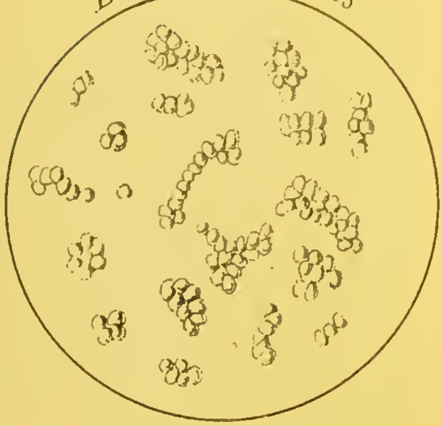

FIG. 3.

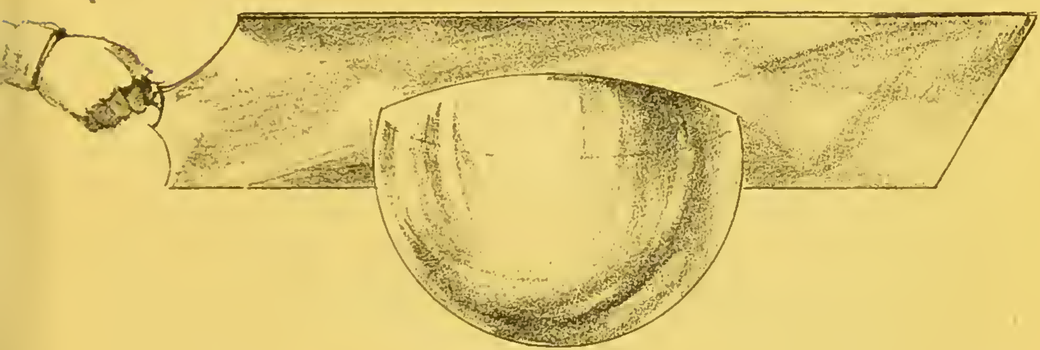

FIG. 4.

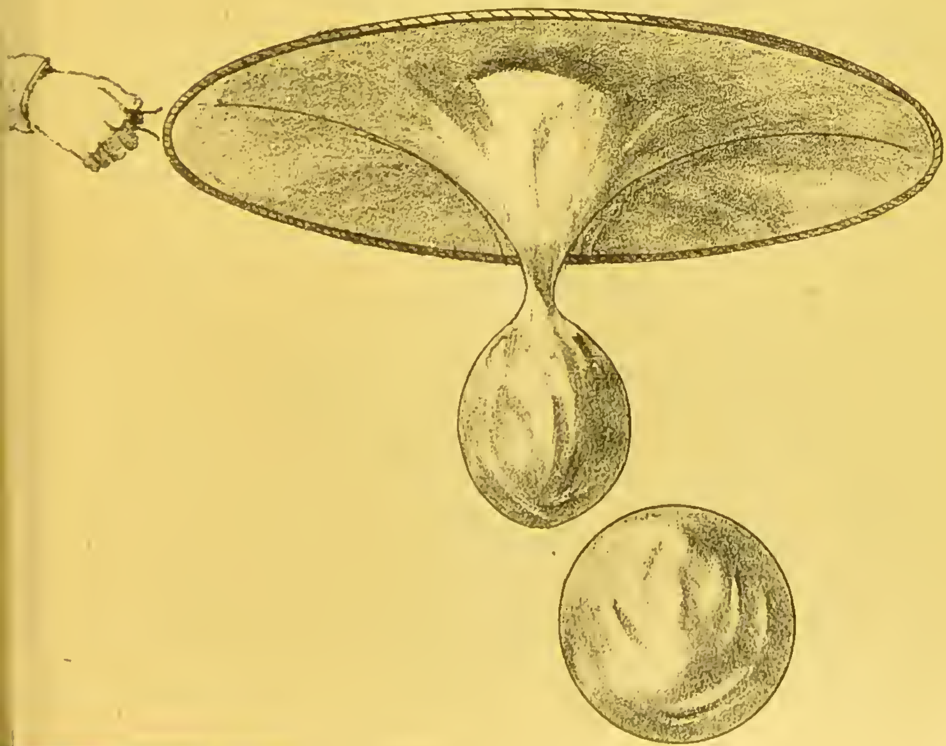

FIG. 1

FIG. 2

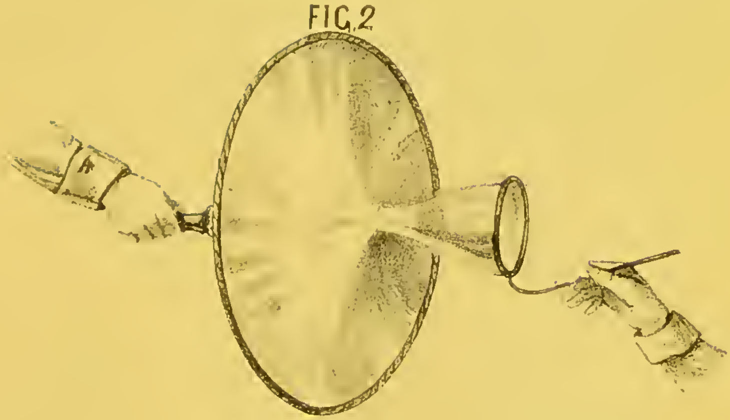

FIG. 3

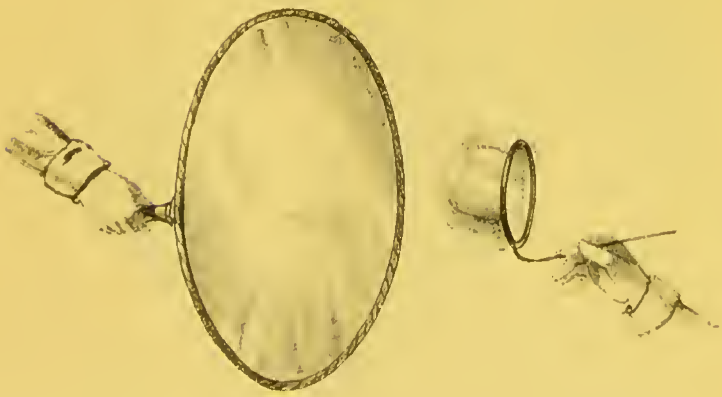

PLATE 6

FIG. 1

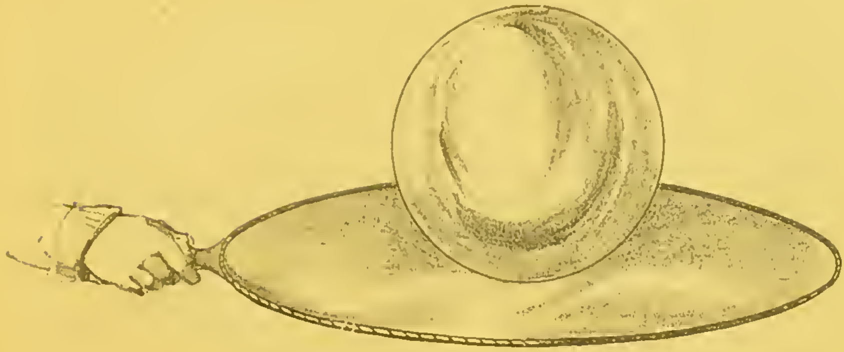

FIG. 2.

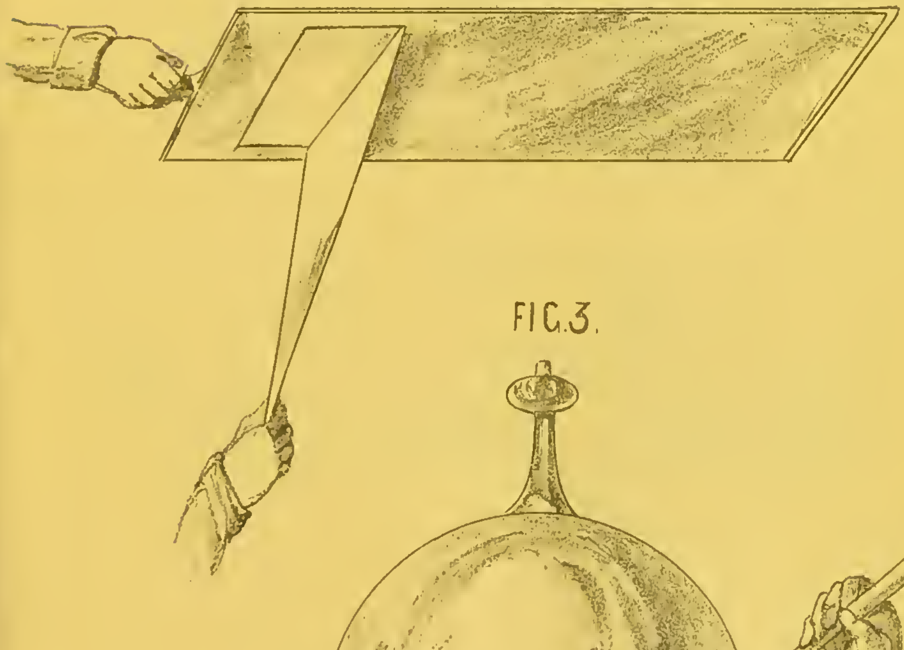

FIG. 3.

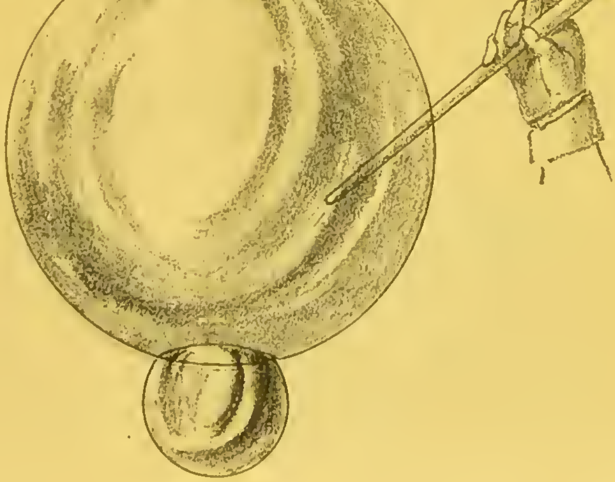

FIG.1.

FIG.2.

FIG.3.

FIG.4.

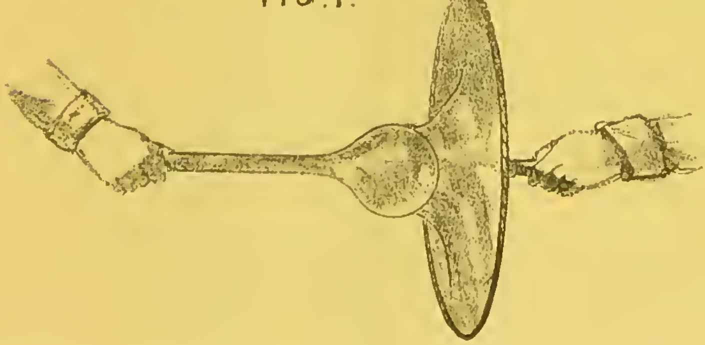

FIG. 1

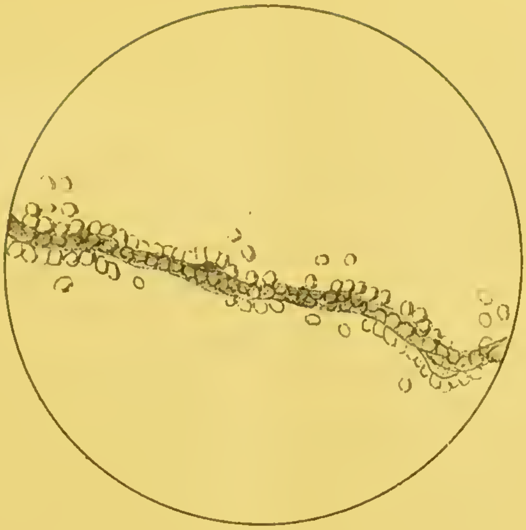

FIG. 2.

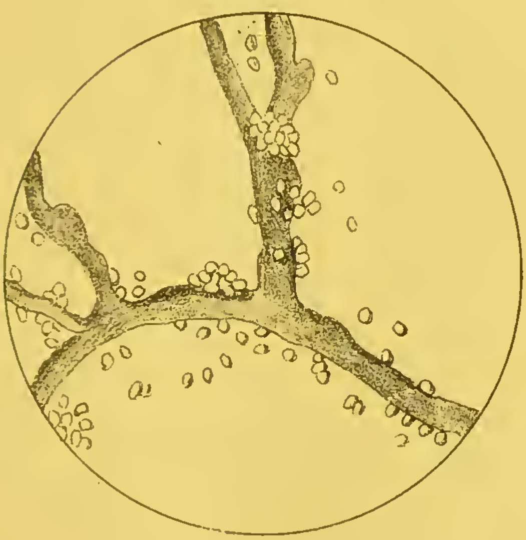

FIG. 3.